REMARKS

Claims 1-7 and 16-18 are pending in this application. Claims 8-15 and 19 were previously canceled without prejudice or disclaimer. No claims are amended herein and, therefore, there is no new matter. Applicant respectfully requests reconsideration and timely allowance of this application in view of the following remarks.

FORMAL MATTERS

Applicant respectfully acknowledges the Office's acceptance of the claim to benefit of priority to Japanese Application 2002-065880, filed March 11, 2002. *See* Office Action at p. 2. Applicant also respectfully acknowledges the Office's withdrawal of the rejection of claims 1-7 under 35 U.S.C. § 112, ¶ 1 and the rejections of claims 1-4, 6, 7, and 16-18 under 35 U.S.C. §§ 102(b) and (e). Office Action at pp. 3-4. Finally, Applicant also notes that page 10 of the Office Action states:

> Regarding eliminating the host genome's pyruvate decarboxylase gene by replacing it with a DNA cassette which includes "a DNA for coding a foreign protein having lactate dehydrogenase activity operably linked to a functional homologue of the genome promoter of the pyruvate decarboxylase gene," it would have been obvious because of a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.

To ensure an accurate record, Applicant respectfully clarifies that the phrase "a DNA for coding a foreign protein having lactate dehydrogenase activity operably linked to a functional homologue of the genome promoter of the pyruvate decarboxylase gene," quoted by the Office on page 10 of the Office Action does not appear in the claims, specification, or any of the previously-filed responses and, therefore, does not refer to any of Applicant's statements or claims on the record.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103

Claims 1-7 and 16-18 are rejected under 35 U.S.C. § 103 as allegedly being obvious over WO 99/14335 to Porro et al. ("*Porro*"). *See* Office Action at pp. 4-11. Specifically, although the Office acknowledges that "Porro et al. does not teach knocking out the host genome's pyruvate decarbyxylase gene by introducing a gene expression cassette in its place," the Office contends that the claimed invention is obvious because "all of the claimed elements were known in the prior art and one skilled in the art could have combined the element[s] as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention." *Id.* at pp. 9-10. Applicant respectfully traverses.

The Office must make several basic factual inquiries to determine whether the claims of a patent application are obvious under 35 U.S.C. § 103. These factual inquiries, set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966), require the Office to:

(1) determine the scope and content of the prior art;

(2) ascertain the differences between the prior art and the claims in issue;

(3) resolve the level of ordinary skill in the pertinent art; and

(4) evaluate evidence of secondary considerations.

The obviousness or non-obviousness of the claimed invention is then evaluated in view of the results of these inquiries. *Graham*, 383 U.S. at 17-18; *see also KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1734 (2007). "To reach a proper determination under 35 U.S.C. § 103, the Examiner must step backward in time and into the shoes

worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made." M.P.E.P. § 2142, 8th Ed., July 2008 Rev. Once the findings of fact are articulated, the Office "must then make a determination whether the claimed invention 'as a whole' would have been obvious at the time to that person." *Id.* The Federal Circuit has stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusions of obviousness." M.P.E.P. § 2142 (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)); *see also KSR*, 127 S. Ct. at 1741 (quoting Federal Circuit statement with approval).

In addition to the "teaching-suggestion-motivation" test, the M.P.E.P. offers six exemplary rationales that may support a conclusion of obviousness, all of which require an element of predictability. *See* M.P.E.P. § 2143. Here, the Office appears to rely on the rationale that the instant invention allegedly combines "prior art elements according to known methods to yield predictable results." *Id.* However, Applicant respectfully submits that the Office has not made a *prima facie* case of obviousness because it has failed to establish that the instant invention yields predictable results based on the teachings of *Porro*.

Porro teaches that the recombinant yeast disclosed therein produce 43.1 g of lactic acid per liter of culture solution after 92 hours of fermentation and 109 g of lactic acid per liter of culture solution after 137 hours of fermentation. *See Porro* at Tables B and 6 on pages 52 and 61, respectively. *Porro* also teaches that the recombinant yeast examined in Tables B and 6 were produced by electroporation with exogenous 2μm plasmids encoding a foreign lactate dehydrogenase gene. *See*, *e.g.*, *Porro* at p. 13, ln

10-p. 14, ln. 15; p. 30, ln. 7-p. 31, ln. 15; and p. 41 ln. 25-p. 44, ln. 8. Since electroporated cells generally contain 30-50 copies of exogenous 2μm plasmids (*see, e.g.*, Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd ed. at Chapter 16, and Ausubel et al., Current Protocols in Molecular Biology, Vol. 2 at Chapter 13), the yeast disclosed in *Porro* likely contain several copies of the foreign lactate dehydrogenase gene.

In contrast, an embodiment of the claimed invention in which the transformed yeast contained only a single integrated copy of the foreign lactate dehydrogenase gene, was capable of producing 45.0 to 50.0 g of lactic acid per liter of culture solution after 120 hours of fermentation. *See* specification at [0063]. Thus, with incorporation of only a single copy of a lactate dehydrogenase gene, the recombinant yeast of the instant invention produce quantities of lactic acid similar to those produced by the yeast disclosed in *Porro*, which contain multiple lactate dehydrogenase genes. Based on the teachings of *Porro*, one skilled in the art could not have predicted the increased efficiency of lactic acid production revealed by the instant invention. Since the results of the claimed invention were not predictable from the prior art, the Office has failed to establish a *prima facie* case of obviousness.

For at least these reasons, Applicant submits that the instantly claimed invention is not obvious in view of *Porro*. Accordingly, Applicant respectfully requests that the rejection of claims 1-7 and 16-18 under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

If the Office believes a telephone call would be useful in resolving any outstanding issues, the Office is respectfully invited to call the undersigned at the number listed below.

Please grant any extensions of time required to enter this response and charge any required fees that are not found with this Amendment to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: December 29, 2008

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